



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: February 28, 2002

SUBJECT: **Endosulfan.** Anticipated Residues, and Revised Acute and Chronic Dietary Exposure Analyses.
Reregistration Case No.: 819236.
PC code: 079401.
DP Barcode No.: D281201.

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ACTION REQUESTED

Revised probabilistic Tier 3 (Monte-Carlo) acute dietary and chronic dietary exposure assessments for endosulfan were requested to estimate the dietary risks associated with the reregistration of endosulfan. It was requested that these assessments incorporate results from the United States Department of Agriculture's (USDA's) Pesticide Data Program (PDP) when available. Endosulfan residue estimates used in this assessment include endosulfan (alpha and beta isomers) and endosulfan sulfate along with the percent crop treated (%CT) estimates reported by the Biological and Economic Analysis Division (BEAD). The anticipated residue (AR) estimates are based primarily on three data sources: 1) USDA PDP food sampling data; 2) Food and Drug Administration (FDA) Surveillance Monitoring data; and 3) field trial data, submitted by the registrant to support tolerances.

The content of this memo has been reviewed and approved by the Health Effects Division's Chemistry Science Advisory Council and Dietary Exposure Science Advisory Council.

EXECUTIVE SUMMARY

The acute and chronic dietary risk assessments were conducted for all supported endosulfan food uses. Dietary risk estimates are provided for the general U.S. population and various population subgroups, with the major emphasis placed on the exposure estimates for infants and children. This assessment concludes that for all supported registered commodities, the acute risk estimates are above the Agency's level of concern (<100% aPAD¹) at the 99.9th exposure percentile for the infants less than 1 year of age (105% aPAD), children 1-6 years of age (170% aPAD), and children 7-12 years of age (111% aPAD). This assessment also concludes that for all commodities, the chronic risk estimates are below the Agency's level of concern (<100% cPAD) for the U.S. population (<1% of the cPAD) and all population subgroups with the highest exposed population subgroup, children 1-6 years of age (19% cPAD).

TOXICOLOGICAL INFORMATION

HED has completed a revision of the dietary risk assessment for endosulfan using updated methods for estimating acute dietary exposure. Based on the deliberations of the Hazard Identification Assessment Review Committee (HIARC), hazard endpoints have been selected for both acute (one day) and chronic (long term) exposure intervals (*Memorandum*: D. Liem and J. Rowland to S. DeVito dated October 7, 1998).

An uncertainty factor (UF) of 100 was applied to both acute and chronic risk assessments to account for inter-species extrapolation and intra-species variability. The FQPA

¹aPAD/cPAD = acute/chronic Population Adjusted Dose = $\frac{\text{Acute or Chronic RfD}}{\text{FQPA Safety Factor}}$

Safety Factor committee concluded that an FQPA safety factor of 10X is required for the U.S. general population and all population subgroups (*Memorandum*: B. Tarplee dated February 14, 2002).

Acute Dietary Toxicity Endpoint:

The toxicity endpoint for the acute dietary risk assessment was selected from an acute oral neurotoxicity study in rats where there was an increased incidence of stilted gait, straddled hind-limbs, irregular respirations, panting and decreased motor activity in female rats given a single dose of 3.0 mg/kg (LOAEL); the NOAEL was 1.5 mg/kg. To derive the acute reference dose (acute RfD), an uncertainty factor (UF) of 100 was applied to the doses selected for risk assessment to account for both interspecies extrapolation and intra-species variability. An additional factor of 10X was retained for the U.S. general populations and all population subgroups in accordance with the FQPA for dietary risk assessment. The acute RfD was adjusted to account for the FQPA safety factor to derive the population adjusted dose (acute PAD).

$$\begin{aligned} \text{Acute RfD} &= \frac{\text{NOAEL}}{\text{UF}} = \frac{1.5 \text{ mg/kg}}{100} & \text{aPAD} &= \frac{\text{acute RfD}}{\text{FQPA safety Factor}} = \frac{0.015}{10} \\ &= \mathbf{0.015 \text{ mg/kg}} & &= \mathbf{0.0015 \text{ mg/kg}} \end{aligned}$$

Chronic Dietary Risk Assessment:

The toxicity endpoint for the chronic dietary risk assessment was selected from a 2-year dietary toxicity study in rats where decreased body weight gain and kidney toxicity occurred in male rats at 2.9 mg/kg (LOAEL; the NOAEL was 0.6 mg/kg. To derive the chronic reference dose (chronic RfD), an uncertainty factor (UF) of 100 was applied to the doses selected for risk assessment to account for both interspecies extrapolation and intraspecies variability. An additional factor of 10X was retained for the U.S. general populations and all population subgroups in accordance with the FQPA for dietary risk assessment. The chronic RfD was adjusted to account for the FQPA safety factor to derive the population adjusted dose (chronic PAD).

$$\begin{aligned} \text{Chronic RfD} &= \frac{\text{NOAEL}}{\text{UF}} = \frac{0.6 \text{ mg/kg}}{100} & \text{cPAD} &= \frac{\text{Chronic RfD}}{\text{FQPA safety Factor}} = \frac{0.006}{10} \\ &= \mathbf{0.006 \text{ mg/kg}} & &= \mathbf{0.0006 \text{ mg/kg}} \end{aligned}$$

Table 1. Summary of the Toxicological endpoints for endosulfan.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL=1.5	Increased incidences of convulsions seen within 8 hours after dosing in females	Acute neurotoxicity-Rat
	UF=100 FQPA = 10X	Acute RfD = 0.015 mg/kg aPAD = 0.0015 mg/kg	
Chronic Dietary	NOAEL= 0.6	Reduced body weight gain and increased incidences of marked progressive glomerulonephrosis and blood vessel aneurysms in male rats	2-year chronic toxicity/ carcinogenicity-Rat
	UF=100 FQPA = 10X	Chronic RfD = 0.006 mg/kg/day cPAD = 0.0006 mg/kg	

CONSUMPTION DATA AND DIETARY RISK ANALYSIS

The DEEM™ Program: HED is currently using software developed by Novigen Sciences, Inc. to calculate acute and chronic dietary risk estimates for the general U.S. population and various population subgroups. The food consumption data used in the program are taken from the USDA Continuing Survey of Food Intake by Individuals (CSFII). The Agency is currently using 1989-92 consumption data. Consumption data are averaged for the entire U.S. population, and within population subgroups such as “all infants” to support chronic risk assessment, but retained as individual daily consumption data points to support acute risk assessment (which is based on distributions of consumption estimates for either deterministic- or probabilistic-type exposure estimates). The DEEM™ software is capable of calculating probabilistic type risk assessments when appropriate residue data (distribution of residues) are available.

For acute risk assessments, one-day consumption data are summed and a food consumption distribution is calculated for each population subgroup of interest. The consumption distribution can be multiplied by a residue point estimate for a deterministic (Tier I/II type) exposure/risk assessment, or used with a residue distribution in a probabilistic (Monte Carlo) type risk assessment. Exposure estimates are expressed in mg/kg bw/d and as a percent of the aPAD.

For chronic risk assessments, residue estimates for foods (e.g. apples) or food-forms (e.g. apple juice) of interest are multiplied by the averaged consumption estimate of each food/food-form of each population subgroup. Exposure estimates are expressed in mg/kg bw/d and as a percent of the cPAD.

RESIDUE INFORMATION

Endosulfan Use:

Endosulfan is an insecticide and acaricide which acts as a poison to a wide variety of insects and mites on contact. Technical grade endosulfan is a mixture of two geometric isomers of a synthetic chlorinated cyclodiene, the alpha and beta isomers. These isomers are in a ratio of 70:30, respectively. Endosulfan is currently registered for food/feed uses on a variety of field, fruit, and vegetable crops. In a meeting held on April 21, 1997 the Metabolism Assessment Review Committee (MARC) concluded that the residues of toxicological concern are endosulfans and the sulfate metabolite; therefore, tolerances for crop and livestock commodities should be expressed as residues of the parent and the sulfate metabolite. The MARC also recommended that the tolerance expression be revised to specify the alpha- and beta- isomers of endosulfan. The published tolerances for endosulfan (alpha and beta isomers) [6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3-oxide] and its metabolite endosulfan sulfate [6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepin-3,3-oxide] are listed in 40 CFR §180.182.

Acute Assessment:

The PDP and FDA databases report the majority of detected residues as residues found in 5 lb. (PDP) and 5-20lb. (FDA) composite samples. This manner of reporting may not be representative of possible high-end residues that could be found if individual units of fruits and vegetables were analyzed. This assessment uses statistical methodology for applying existing (composite) information to acute dietary risk assessments. This methodology consists of extrapolating data on pesticide residues in composite samples of fruits and vegetables to residue levels in single servings of fruits and vegetables. Given the composite sample mean, the composite sample variance, the number of units in each composite sample, and assuming a lognormal distribution, it is possible to *estimate* the mean and variance of the pesticide residues present on single servings of fruits and vegetables. These parameters can then be applied to generate information on the level of residue in fruits and vegetables (and calculate a theoretical distribution). This information was incorporated into a probabilistic exposure estimation model, the Monte-Carlo method. This methodology has a higher degree of accuracy when more than 30 composite samples have detectable residues (Use of Pesticide Data Program in Acute Risk Assessment - sent to Federal Register May, 1999). Commodities that are blended (such as grains) or are smaller than single unit servings (peas) were not decomposed since the measured PDP levels were assumed representative of the actual range of residue.

Chronic Assessment:

For chronic risk assessment, reported residues were averaged, whether based on PDP, FDA, or field trials. If a commodity had no reported detections by the PDP and FDA programs, and the expectation of no detection was confirmed by field trial data, the weighted average of the limit of detection (LOD) was used to account for possible exposure that could not be more precisely quantified ($\frac{1}{2}$ LOD alpha-endosulfan + $\frac{1}{2}$ LOD beta-endosulfan + $\frac{1}{2}$ LOD endosulfan sulfate). For commodities with no

detections from FDA data, half the limit of quantitation (LOQ) was used for alpha-endosulfan, beta-endosulfan, and endosulfan sulfate. The weighted average estimate of percent crop treated (%CT) was incorporated into all chronic residue estimates.

Endosulfan (alpha and beta isomers) and Endosulfan Sulfate:

This assessment assumes that endosulfan (alpha and beta isomers) and endosulfan sulfate are equal in toxicity. In general, field trial studies have included analyses for both isomers of endosulfan as well as endosulfan sulfate, as have FDA surveillance data and PDP data. For the commodities in which alpha-endosulfan, beta-endosulfan or endosulfan sulfate were detected in the field trial analyses, FDA surveillance, or by PDP, the non-detected compounds are accounted for by an assumption of ½ LOD (PDP data and field trial data) or ½ LOQ (FDA data).

Processing Factors:

Endosulfan residues may be either concentrated or reduced by the activities of drying (prunes etc.), processing (juice, catsup, etc.), washing, peeling, and cooking; since processing data was limited, the Dietary Exposure Evaluation Model (DEEM™) default factors were used in this assessment for most commodities (see Attachments 3 and 5). Acceptable processing studies were available for apples, cottonseed, grapes, pineapples, potatoes, and tomatoes. A processing factor of 1X was used for grape juice (MRID Nos. 00156259 and 44346915), pineapple juice (MRID No. 00157147), and tomato puree (MRID Nos. 00146842 and 44346914). A processing factor of 3.7X was used for pineapple concentrate and a factor of 1.2X was used for tomato paste (MRID Nos. 00146842 and 44346914).

Additional Refinements:

The Health Effects Division has developed procedures for handling FDA surveillance monitoring data in dietary exposure analyses with the goal of generating more realistic Tier 3 dietary exposure estimates by features of version 7 DEEM software. Version 7 DEEM software now permits non-representative, stratified sampling of data to be incorporated into dietary risk assessments. Currently the use of FDA surveillance monitoring data and its incorporation into HED risk assessments is “case-by-case” relying on the judgement of the reviewer and depends on the degree of over-sampling of imported produce, observed, the differences in residue concentrations between domestic and imported produce and the sample size. If there are significant differences between domestic and import samples, either in terms of likelihood of detected residues or residue levels themselves, then it would be most desirable to “weight” the FDA data such that it better reflects the proportionate “mix” between domestic and foreign produce which the U.S. population consumes. Additional estimates of the percent of commodity imported as well as imported %CT from BEAD are also incorporated. The crops that incorporate these procedures are dried beans, blueberries, cauliflower, cherries, fresh sweet corn, cucumbers, melons (except cantaloupe), fresh succulent peas, peppers, pineapples, plums, pumpkins, and summer squash. The additional refinements include modifications to the above mentioned crops only.

Residue Estimates for Crops:

Dietary risk estimates are based, in part, on estimates of the percent usage of endosulfan on each registered crop. BEAD has estimated endosulfan use (Quantitative Usage Analysis for Endosulfan from S. Nako to S. DeVito dated October 13, 1999) based on available pesticide survey usage data for the years 1987 through 1998 (Attachment 7). BEAD estimates are provided to HED as a weighted average and as an estimated maximum. This risk assessment assumed 1% crop treated for any BEAD estimate less than 1%. The estimated maximum %CT for each commodity was used for the acute risk assessment and the estimated weighted average %CT for each commodity for the chronic dietary risk assessments. Where no further information was available, 100 %CT was assumed (Attachments 1 and 2).

Endosulfan residue estimates, or ARs in this assessment are based primarily on three data sources: 1) field trial data, submitted by the registrant to support tolerances; 2) USDA PDP food sampling data; and 3) FDA Surveillance Monitoring data. Where data were not available, tolerance levels were used incorporating the %CT estimates from BEAD. The order of preference for the purpose of risk assessment is: PDP data > FDA data > field trial data > tolerance. PDP data are preferred over FDA data because the statistical design of the PDP program is specific for dietary risk assessment (i.e. sampling is done at grocery store distribution points instead of directly from the field), and because the foods are prepared before analysis as they would typically be before consumption (i.e. peeling, washing). Many endosulfan treated commodities not sampled by the PDP program are assessed based on translation of data from PDP sampled commodities in the same crop group, FDA surveillance data, or field trial data where available. Tolerance values were used for sugarcane and watercress. Field trial residue data are generally considered by HED as an upper-end or a worse case scenario of possible residues and are more suited to the requirements of tolerance setting, because it requires highest rates of application and shortest PHI, than to the requirements of dietary risk assessment (when the most realistic estimate is desired).

All endosulfan residue estimates for crop commodities are listed in Attachment 2. The following is a description of how the available data, listed in attachment 1, were utilized on a crop by crop basis:

Almonds: Field trial data were used directly incorporating the maximum %CT for uncooked, cooked, baked, boiled, dried, and frozen food forms (MRID Nos.: 00003713, 00004254). Little or no monitoring data are available.

Apples: Three years of PDP data were decomposited² incorporating the maximum %CT

² Decompositing consists of extrapolating from data on pesticide residues in composite samples of fruits and vegetables to residue levels in single units of fruits and vegetables. Data is decomposited when there are 30 samples or more with detectable residues.

for uncooked, cooked, baked, boiled, and fried food forms. For canned and frozen apples, the PDP data were used directly incorporating the maximum %CT. The average from apple PDP data was used incorporating the apple maximum %CT for the dried apples food form, and apple juice used three years of PDP juice data directly incorporating the apple maximum %CT. Five years of FDA data on fresh apples and apple juice were used to support the findings in PDP data.

Apricots: Three years of peach PDP data were decomposited and translated incorporating the apricot maximum %CT for uncooked, cooked, and boiled food forms. For canned and dried apricots and apricot juice, the peach PDP data was translated and used directly incorporating the apricot maximum %CT. The FDA data available for apricots was considered inappropriate to use; therefore, it was the decision of the dietary exposure assessment science advisory council to translate peach data to apricots.

Barley: Three years of wheat PDP data were averaged incorporating the barley maximum %CT and translated to all barley food forms. FDA data suggest that residues found in/on barley are similar to those found in/on wheat.

Beans-

Dry: Five years of FDA data were used directly for all food forms of dried beans with no further adjustment for %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used for all food forms with no further adjustment for import or domestic %CT.

Succulent: Three years of PDP data on fresh beans were used directly incorporating fresh snap bean maximum %CT for all uncooked, cooked, and boiled beans except lima beans. Two years of PDP data for canned beans were used directly incorporating processed snap bean maximum %CT for all canned beans. Two years of PDP data for frozen beans were used directly incorporating fresh snap bean maximum %CT for all frozen beans except lima beans. Five years of FDA data on fresh beans were used to support the findings in PDP data.

Blueberries: Five years of FDA data were used directly incorporating the maximum %CT for uncooked, cooked, baked, boiled, canned, and frozen food forms. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used for all food forms incorporating the maximum domestic %CT and the import %CT.

Broccoli: One year of PDP data was used directly incorporating the maximum %CT. Five years of FDA data on fresh broccoli were used to support the findings in PDP data.

Brussels Sprouts: One year of lettuce PDP data was translated to all food forms of Brussels sprouts using lettuce data directly incorporating brussels sprout maximum %CT; however, FDA data suggest that the residues likely to be found in/on brussels sprouts

would be less than those found in/on lettuce.

Cabbage: One year of broccoli PDP data was translated and used directly incorporating the fresh cabbage maximum %CT for uncooked, cooked, baked, boiled, and fried food forms. For canned and cured cabbage, the broccoli PDP data was translated and used directly incorporating the processed cabbage maximum %CT. The FDA data available for cabbage were considered inappropriate to use; therefore, it was the decision of the dietary exposure assessment science advisory council to translate surrogate data to cabbage. However, in the additional assessments, FDA data for cabbage were separated according to sample origin (domestic vs. import), weighted based on %imported and used for all food forms incorporating the maximum domestic %CT and the import %CT.

Carrots: Three years of PDP data were decomposed incorporating the maximum %CT for uncooked, cooked, baked, and boiled food forms. For canned and frozen carrots, the PDP data were used directly incorporating the maximum %CT. Five years of FDA data on fresh carrots were used to support the findings in PDP data.

Cauliflower: Five years of FDA data were used directly incorporating the maximum %CT for uncooked, cooked, boiled, fried and frozen food forms. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used for all food forms incorporating the maximum domestic %CT and the import %CT.

Celery: One year of PDP data was used directly incorporating the maximum %CT for uncooked, cooked, baked, boiled, fried, canned, frozen, and juice food forms. Five years of FDA data on fresh celery were used to support the findings in PDP data.

Cherries: Five years of FDA data were used directly incorporating the sweet cherry maximum %CT for fresh uncooked, cooked, baked, and boiled cherries. For canned, frozen, and dried cherries as well as cherry juice, the FDA data were used directly incorporating the tart cherry maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used for all food forms incorporating the maximum domestic, tart and sweet cherry, %CT and the import %CT.

Collards: Four years of spinach PDP data were translated to all collard food forms using spinach data directly incorporating the collard maximum %CT; however, FDA data suggest that the residues likely to be found in/on collards would be less than those found in/on spinach.

Corn-

Sweet: Five years of FDA data were used directly incorporating the maximum %CT for uncooked, cooked, baked and boiled food forms. For canned sweet corn, three years of canned sweet corn PDP data were used directly incorporating the maximum %CT. For frozen sweet corn, three years of frozen sweet corn PDP data were used directly incorporating the maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin

(domestic vs. import), weighted based on %imported, and used for uncooked, cooked, baked and boiled food forms incorporating the maximum domestic %CT and the import %CT.

Cottonseed: Field trial data were averaged incorporating the maximum %CT for refined oil and meal (MRID Nos.: 44854101 and 44854102). Little or no monitoring data are available.

Cucumbers: Five years of FDA data were decomposited incorporating the maximum %CT for uncooked cucumbers. For canned cucumbers, the FDA data were used directly incorporating the maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked cucumbers incorporating the maximum domestic %CT and the import %CT. For canned cucumbers, all five years of FDA data were weighted according to %imported and used directly incorporating the maximum domestic %CT and the import %CT.

Eggplant: Two years of tomato PDP data were decomposited and translated to all eggplant food forms incorporating the eggplant maximum %CT; however, FDA data suggest that the residues likely to be found in/on eggplants would be less than those found in/on tomatoes.

Filberts: Field trial data were used directly incorporating %CT for uncooked, baked, and boiled food forms (MRID No.: 00004254). Little or no monitoring data are available.

Grapes: Three years of PDP data were used directly incorporating the maximum %CT for uncooked, cooked, canned, frozen and dried food forms. Five years of FDA data on fresh grapes were used to support the findings in PDP data. For grape juice, one year of PDP data were used directly incorporating the grape maximum %CT. Five years of FDA data on grape juice were used to support the findings in the PDP juice data.

Kale: One year of broccoli PDP data was translated to all kale food forms using broccoli data directly and incorporating the maximum %CT. FDA data suggest that residues found in/on kale are similar to those found on broccoli.

Lettuce: One year of PDP data was decomposited incorporating the maximum %CT for uncooked head lettuce. For uncooked leafy lettuce and canned lettuce, the PDP data were used directly incorporating the maximum %CT. Five years of FDA data on both fresh head and fresh loose-leaf lettuce were used to support the findings in PDP data.

Macadamia Nuts: Field trial data were used directly incorporating %CT for baked macadamia nuts (MRID No.: 00004254). Little or no monitoring data are available.

Melons-

Cantaloupe: One year of PDP data was decomposited incorporating the cantaloupe maximum %CT for uncooked cantaloupe; although only 26 samples in the PDP data showed detectable residues, the data were decomposited due to the supporting FDA data demonstrating 276 detectable residues out of 655 samples tested. For cantaloupe juice, the PDP data was used directly incorporating the cantaloupe maximum %CT. Five years of FDA data on fresh cantaloupe were used to support the findings in PDP data.

Honeydew: Five years of FDA data were decomposited incorporating the honeydew maximum %CT for uncooked honeydew melons. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked honeydew melons incorporating the maximum domestic %CT and the import %CT.

Other: Five years of honeydew FDA data were decomposited and translated to all other melon food forms incorporating the other melon maximum %CT. In the additional assessments, all five years of honeydew FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for all other melon food forms incorporating the maximum domestic %CT and the import %CT.

Watermelons: Five years of FDA data were decomposited incorporating the watermelon maximum %CT for uncooked watermelons. For watermelon juice, the FDA data were used directly incorporating the watermelon maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked watermelons incorporating the maximum domestic %CT and the import %CT. For watermelon juice, all five years of FDA data were weighted according to %imported and used directly incorporating the maximum domestic %CT and the import %CT.

Mustard Greens: Four years of spinach PDP data were translated to all mustard green food forms incorporating the mustard green maximum %CT. FDA data suggest that the residues likely to be found in/on mustard greens are similar to those found in/on spinach.

Nectarines: Three years of peach PDP data were decomposited and translated incorporating the nectarine maximum %CT for uncooked nectarines. The FDA data available for nectarines was considered to be inappropriate to use directly; therefore, it was the decision of the dietary exposure assessment science advisory council to translate peach data to nectarines.

Oats: Three years of wheat PDP data were averaged incorporating the oat maximum %CT and translated to all oat food forms. FDA data suggest that residues found in/on oats are similar to those found in/on wheat.

Peaches: Three years of PDP data were decomposited incorporating the maximum %CT for uncooked, cooked, baked, and boiled food forms. For frozen and dried peaches as well as peach juice, the PDP data were used directly incorporating the maximum %CT. For canned peaches, one year of PDP data on canned peaches was used directly incorporating the maximum %CT. Five years of FDA data on fresh peaches and peach juice were used to support the findings in PDP data.

Pears: Two years of PDP data were decomposited incorporating the maximum %CT for uncooked, cooked, baked, and boiled food forms. For canned and dried pears as well as pear juice, the PDP data were used directly incorporating the maximum %CT. Five years of FDA data on fresh pears and pear juice were used to support the findings in PDP data.

Peas-

Succulent: Five years of FDA data for fresh peas were used directly incorporating the maximum %CT for all uncooked, cooked, baked, boiled, and fried peas. Three years of PDP data for canned peas were used directly incorporating the maximum %CT for all canned peas. Three years of PDP data on frozen peas were used directly incorporating the maximum %CT for all frozen peas. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used directly for all uncooked, cooked, baked, boiled, and fried peas incorporating the maximum domestic %CT and the import %CT.

Pecans: Filbert field trial data were translated to all pecan food forms directly incorporating the pecan maximum %CT. Little or no monitoring data are available.

Peppers-

Hot: Five years of hot pepper FDA data were decomposited incorporating the hot pepper maximum %CT for uncooked, cooked, baked, boiled, and fried food forms. For canned, frozen, and cured hot peppers, the FDA data were used directly incorporating the hot pepper maximum %CT. In the additional assessments, all five years of hot pepper FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked, cooked, baked, boiled, and fried food forms incorporating the maximum domestic %CT and the import %CT. For canned, frozen, and cured hot peppers, all five years of FDA data were weighted according to %imported and used directly incorporating the maximum domestic %CT and the import %CT.

Other: Five years of bell pepper FDA data were decomposited incorporating the pepper maximum %CT for all other pepper food forms excluding black pepper. In the additional assessments, all five years of bell pepper FDA data were separated according to sample origin (domestic vs. import), weighted based on

%imported, decomposited, and used for all other pepper food forms excluding black pepper and incorporating the maximum domestic %CT and the import %CT.

Sweet: Five years of bell pepper FDA data were decomposited incorporating the sweet pepper maximum %CT for uncooked, cooked, baked, and boiled food forms. For canned, frozen, and cured sweet peppers, the FDA data were used directly incorporating the sweet pepper maximum %CT. In the additional assessments, all five years of bell pepper FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked, cooked, baked, and boiled food forms incorporating the maximum domestic %CT and the import %CT. For canned, frozen, and cured sweet peppers, all five years of FDA data were weighted according to %imported and used directly incorporating the maximum domestic %CT and the import %CT.

Pineapples: Five years of FDA data were used directly incorporating the maximum %CT for uncooked, cooked, baked, boiled, canned and frozen food forms as well as pineapple juice. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used directly for uncooked, cooked, baked, boiled, canned and frozen food forms as well as juice incorporating the maximum domestic %CT and the import %CT.

Pistachio: Almond field trial data were translated and used directly assuming 100%CT for uncooked, cooked, and baked food forms (MRID Nos.: 00003713, 00004254). Little or no monitoring data are available.

Plums: Five years of FDA data were used directly incorporating the fresh plum maximum %CT for uncooked, cooked, canned, frozen and cured food forms. For prunes (dried plums), the FDA data were used directly incorporating the prune maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used directly for uncooked, cooked, baked, boiled, canned, frozen and cured food forms incorporating the maximum domestic %CT and the import %CT. For prunes (dried plums), all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, and used directly incorporating the maximum domestic prune %CT and the import prune %CT.

Potatoes-

White/Irish: Two years of PDP data were decomposited incorporating the maximum %CT for cooked, baked, boiled, and fried food forms. For canned and frozen potatoes, the PDP data were used directly incorporating the maximum %CT. For dried potatoes, the average of PDP data were used with no further adjustment for %CT incorporating LOQ for all non-detectable residues. Five

years of FDA data on fresh potatoes were used to support the findings in PDP data.

Sweet: Three years of PDP data were used directly incorporating the maximum %CT for cooked, baked, boiled, fried, and canned food forms.

Pumpkins: Five years of cucumber FDA data were decomposited and translated to cooked, baked, boiled, and fried pumpkins incorporating the pumpkin maximum %CT. For canned pumpkins, the cucumber FDA data were translated and used directly incorporating the pumpkin maximum %CT. In the additional assessments, all five years of cucumber FDA data were separated according to sample origin (domestic vs. import), weighted based on % pumpkin imported, decomposited, and translated to cooked, baked, boiled, and fried pumpkins incorporating the maximum domestic pumpkin %CT and the import pumpkin %CT. For canned pumpkin, all five years of cucumber FDA data were weighted according to %pumpkin imported and used directly incorporating the maximum domestic pumpkin %CT and the import pumpkin %CT.

Rye: Three years of wheat PDP data were averaged incorporating the rye maximum %CT and translated to all rye food forms. FDA data suggest that residues found in/on rye are similar to those found in/on wheat.

Soybeans: Five years of FDA data were averaged incorporating the adjustment for %CT for all food forms.

Spinach: Four years of PDP data for fresh spinach were used directly incorporating the maximum %CT for uncooked, cooked, boiled, and frozen food forms. For canned spinach, one year of PDP data for canned spinach was used directly incorporating the maximum %CT. Five years of FDA data on fresh spinach were used to support the findings in PDP data.

Squash-

Summer: Five years of FDA data were decomposited incorporating the squash maximum %CT for uncooked, cooked, baked, boiled, and fried food forms. For canned, frozen, and cured summer squash, the FDA data were used directly incorporating the squash maximum %CT. In the additional assessments, all five years of FDA data were separated according to sample origin (domestic vs. import), weighted based on %imported, decomposited, and used for uncooked, cooked, baked, boiled and fried food forms incorporating the maximum domestic %CT and the import %CT. For canned, frozen, and cured summer squash, all five years of FDA data were weighted according to %imported and used directly incorporating the maximum domestic %CT and the import %CT.

Winter: Five years of PDP data were decomposited incorporating the squash maximum %CT for uncooked, cooked, baked, boiled, and fried food forms.

Strawberries: One year of PDP data was used directly incorporating the maximum %CT for uncooked, cooked, baked, boiled, canned, and frozen food forms. Five years of FDA data on fresh strawberries were used to support the findings in PDP data.

Sugarcane: Tolerance was used incorporating the maximum %CT for all food forms. Little or no monitoring data are available (40 CFR §180.182).

Tea: The tolerance value for dried tea leaves is 24 ppm with less than 0.1 ppm residues in beverage tea; therefore, assuming 100 %CT, a residue value of 0.004 ppm was used for both the acute and chronic dietary assessments (MRID Nos.: 00003744, 00003756; 40 CFR §180.2600). Little monitoring data are available; however, all samples tested show no detectable residues (LOQ of 0.002 ppm).

Tomatoes: Two years of PDP data were decomposited incorporating the fresh tomato maximum %CT for uncooked, baked, boiled, and fried food forms. For frozen tomatoes, the PDP data were used directly incorporating the fresh tomato maximum %CT. For canned and dried tomatoes as well as tomato catsup, paste, puree, and juice, the PDP data were used directly incorporating the processed tomato maximum %CT. Five years of FDA data on fresh tomatoes were used to support the findings in PDP data.

Turnip Greens: Four years of spinach PDP data were translated to all turnip green food forms incorporating the turnip green maximum %CT. FDA data suggest that the residues likely to be found in/on turnip greens are similar to those found in/on spinach.

Turnips Roots: Three years of carrot PDP data were decomposited and translated to all turnip food forms incorporating the turnip maximum %CT; however, FDA data suggest that the residues likely to be found in/on turnips would be less than those found in/on carrots.

Walnuts: Field trial data for almonds were translated to uncooked, cooked, and baked walnut food forms using almond data directly and incorporating walnut maximum %CT (MRID Nos.: 00003713, 00004254). For walnut oil, the almond field trial data were averaged incorporating the walnut maximum %CT. Little or no monitoring data are available.

Wheat: Three years of PDP data were averaged incorporating the maximum %CT for all wheat food forms. Five years of FDA data on wheat grain were used to support the findings in PDP data.

Residue Estimates for Meat and Milk:

Potential transfer of pesticide residues from treated feed items to livestock commodities are estimated by calculating a livestock dietary burden, and are based on livestock

feeding studies conducted at the appropriate dose levels. For endosulfan, HED has estimated a realistic dietary burden to cattle. The estimated dietary burden of endosulfan to beef cattle is 0.172 ppm.. The dietary burden was calculated using the following formula: Dietary burden (ppm) = % of Diet/ % Dry Matter X Anticipated Residue (ppm). Inclusion of these feed items would not result in a dietary burden greater than that calculated in Table 2 shown below.

Table 2. Calculation of maximum ruminant dietary burden for Endosulfan (alpha and beta isomers) and Endosulfan Sulfate.

Feed	% CT	Anticipated Residue (ppm)	% Dry Matter	Beef Cattle	
				% of Diet	Burden (ppm)
Wheat, grain	1%	0.003	89	50	0.002
Potato, culls	16%	0.002	20	30	0.003
Cottonseed Gin By-Product	4%	0.754	90	20	0.167
TOTAL				100	0.172

Note: The maximum %CT estimate is incorporated in the crop anticipated residue estimate.

The dosing levels used in the ruminant metabolism study were 4 ppm, 12 ppm, and 30 ppm, which corresponds to 23X, 70X, and 175X the anticipated maximum dietary burden for beef cattle (reviewed by S. Mason Dec. 10, 1999; MRID No.: 44843702).

The ARs calculated for beef cattle shown in Table 3 are also used in this dietary assessment for goat, horse, rabbit, sheep, and veal.

Table 3. Estimated Residues of Endosulfan (alpha and beta isomers) and Endosulfan Sulfate in tissues of lactating cattle dosed at 4 ppm, 12 ppm, and 30 ppm (MRID No.: 44843702) .

Matrix	Dose (28 Days of Dosing)		
	4 ppm	12 ppm	30 ppm
Muscle	0.05	0.22	0.77
Liver	0.72	2.01	3.21
Kidney	0.08	0.32	0.68
Fat	1.42	4.72	9.92

* Endosulfan (alpha and beta isomers) were accounted for by incorporating 1/2LOD for all non-detectable residues.

HED will use PDP data (1996-97) for milk which shows all residues to be less than the

level of detection (LOD 0.001 ppm). The chronic AR for milk is 0.002 ppm, incorporating ½LOD for parent (alpha and beta isomers) and metabolite (endosulfan sulfate); however, for the acute dietary assessment, a residue data file is used for milk which also incorporates ½LOD for each parent (alpha and beta isomers) and metabolite (endosulfan sulfate). See Attachment 1.

Table 4. Residues of Endosulfan (alpha and beta isomers) and Endosulfan Sulfate in tissues of lactating cattle dosed at 0.171 ppm for 28 consecutive days.

Matrix	Anticipated Residue
Muscle	0.003
Liver	0.026
Kidney	0.004
Fat	0.061
Milk	0.002

Potential transfer of pesticide residues from treated feed items to swine commodities are estimated by calculating a swine dietary burden based on swine feeding studies at the appropriate dose level (reviewed by J. Abbotts Feb. 20, 1992; MRID No.: 00003742). The maximum theoretical dietary burden of endosulfan to pigs is 0.035 ppm. However, inclusion of these feed items would not result in a dietary burden greater than that calculated in Table 5.

Table 5. Calculation of maximum swine dietary burden for Endosulfan

Feed Commodity	% CT	Anticipated Residue (ppm)	% Dry Matter	Swine	
				% of Diet	Burden (ppm)
Wheat, grain	1%	0.003	89	80	0.003
Potato Culls, meal	16%	0.032	20	20	0.032
TOTAL				100	0.035

Note: The maximum %CT estimate is incorporated in the crop anticipated residue estimate. The dietary burden was calculated using the following formula: Dietary burden (ppm) = % of Diet/ % Dry Matter X Anticipated Residue (ppm).

In a swine metabolism study (reviewed by J. Abbotts Feb. 20, 1992; MRID No.: 00003742), three female pigs were fed endosulfan once daily in their dry daily diet at a level of 2 ppm; two additional pigs served as control animals. The treated animals were sacrificed after 27, 54, and 81 days. The results of the swine feeding study are presented

in Table 6. Residues of alpha-endosulfan and endosulfan sulfate were detected only in fatty tissues, while beta-endosulfan was not detected in any tissue. The maximum combined residue, 0.17 ppm, was reported in fat from the rear section after 27 days.

Table 6. Endosulfan-derived residues in tissues following a once daily oral administration of endosulfan to pigs at 2.0 ppm for 27, 54, and 81 days consecutively (MRID No.: 00003742).

Tissue	Residues (ppm) At Various Sacrifice Intervals								
	alpha-Endosulfan			beta-Endosulfan			Endosulfan Sulfate		
	27 Days	54 Days	81 Days	27 Days	54 Days	81 Days	27 Days	54 Days	81 Days
Neck lard	0.01	0.08	0.03	<0.01	<0.01	<0.01	0.05	<0.02	0.04
Fat of the rear area	0.12	0.10	0.07	<0.01	<0.01	<0.01	0.05	<0.02	<0.02
Belly fat	0.01	0.10	0.03	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Omental fat	0.05	0.10	0.03	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Renal fat	0.05	0.09	0.02	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Liver	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Gall	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Spleen	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Kidney	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Lung	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Heart	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Brain	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Spinal cord	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Pancreas	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Blood	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Neck muscle	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Tongue	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02
Ovary	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.02	<0.02	<0.02

The dosing level used in the swine metabolism study was 2.0 ppm, which corresponds to 57X the anticipated maximum dietary burden for pigs. The maximum anticipated residue for pigs is listed in Table 7.

Table 7. Estimated Residues of Endosulfan (alpha and beta isomers) and Endosulfan Sulfate in tissues of pigs dosed at 0.171 ppm.

Matrix	Anticipated Residue
Muscle	0.0004
Liver	0.0004

Matrix	Anticipated Residue
Kidney	0.0004
Fat	0.0022

Residue Estimates for Poultry and Eggs:

No endosulfan tolerances are established in eggs and poultry tissues. A poultry feeding study (1967 MRID No.: 00003840) was evaluated in PP#8F0632. Twenty Leghorn hens were fed technical endosulfan in their daily diet at levels of 0.3 and 3.0 ppm for seven weeks; ten additional hens served as control animals. At the end of the feeding period, the chickens were sacrificed, and eggs and tissues were collected. Sample storage conditions and intervals, prior to analyses, were not reported. Residues were determined using a microcoulometric GC method. The reported limits of detection were 0.05 ppm for the combined residues of both endosulfan isomers, and 0.05 ppm for endosulfan sulfate. Method recoveries were 71-100% (average of 88%) for endosulfan and 70-89% (average of 77%) for endosulfan sulfate. The results of the poultry feeding study are presented below. One sample of cavity fat at the 3-ppm feeding level showed 0.06 ppm residues of the endosulfan isomers; all other tissues showed no detectable (<0.05 ppm) residues of the isomers or the metabolite.

TABLE 8. Endosulfan-derived residues in poultry eggs and tissues following oral administration of endosulfan to laying hens at 0.3 and 3.0 ppm for seven weeks. (MRID 00003840).

Tissues	Residues, ppm		
	alpha-Endosulfan	beta-Endosulfan	Endosulfan Sulfate
0.3 ppm-feeding level			
Eggs	<0.05		<0.05
Eggs (Unlaid)	<0.05		<0.05
Cavity fat	<0.05		<0.05
Body fat	<0.05		<0.05
Muscle	<0.05		<0.05
Hearts	<0.05		<0.05

Livers	<0.05	<0.05
Gizzards	<0.05	<0.05
Intestines	<0.05	<0.05
Tissues	Residues, ppm	
	alpha-Endosulfan	beta-Endosulfan Endosulfan Sulfate
30 ppm-feeding level		
Eggs	<0.05	<0.05
Cavity fat	0.06	<0.05
Body fat	<0.05	<0.05
Muscle	<0.05	<0.05
Hearts	<0.05	<0.05
Livers	<0.05	<0.05
Gizzards	<0.05	<0.05
Intestines	<0.05	<0.05

There are no endosulfan tolerances for poultry. Poultry feeding data suggest that there is no reasonable expectation of finite residues; therefore, eggs and poultry were not included in this dietary assessment (CFR §180.683).

Truncation:

Monitoring data show several over-tolerance residues of endosulfan which have been included in this assessment. The decomposited data was truncated at the theoretical maximum residue value of a single serving sample (based on weight and residues of composite samples, and the weight of a single serving sample).

RESULTS AND DISCUSSION

Acute Probabilistic Exposure Analysis: (Monte-Carlo)

Based on the acute dietary exposure analysis as described above and using an aPAD of 0.0015 mg/kg/d for the U.S. population and all population subgroups. The acute dietary exposure to infants less than 1 year of age, children 1-6 years of age, and children 7-12 years of age exceed the aPAD at the 99.9th exposure percentile (see Table 9). Children 1-6 years have been identified as the most highly exposed population subgroup. Estimated acute dietary exposure to children 1-6 years does not exceed the aPAD at the 95th or 99th exposure percentiles. A complete listing of the acute dietary results is in attachment 4.

Several crops have been identified as making significant contributions to the dietary risk. Residues measured on these crops and the surveyed consumption of these crops, factored together, result in these crops taking up a significant percentage of the aPAD and thereby, making significant contributions to the risk. A number of crops had significant residues from monitoring data and are high consumption items. The significant acute contributors have been identified as cucumbers, garden green peas, potatoes, and succulent green beans. For all the significant contributors, PDP and/or FDA monitoring data have shown measurable residues of endosulfan, some greater than tolerance.

The acute summary table below shows the acute dietary risks to the U.S. population, infants, and children from exposures to all the supported crops. A complete listing of the acute dietary results is in Attachment 4.

Table 9. Acute Dietary Risk Estimates with “Weighted” FDA Data

Population	aPAD	(95th percentile)		(99th percentile)		(99.9th percentile)	
		Exposure	% aPAD	Exposure	% aPAD	Exposure	% aPAD
U.S. Population	0.0015 mg/kg	0.000111	<1	0.000310	2	0.001392	9
All Infants <1 year	0.0015 mg/kg	0.000181	12	0.000391	26	0.001568	105
Children 1-6 years	0.0015 mg/kg	0.000207	14	0.000527	35	0.002547	170
Children 7-12 years	0.0015 mg/kg	0.000140	9	0.000383	26	0.001668	111
Females 13-50 years	0.0015 mg/kg	0.000083	6	0.000259	17	0.001226	82
Males 13-19 years	0.0015 mg/kg	0.000095	6	0.000250	17	0.001114	74
Males 20+ years	0.0015 mg/kg	0.000087	6	0.000255	17	0.001134	76
Seniors 55+ years	0.0015 mg/kg	0.000081	5	0.000285	19	0.001316	88

Chronic Exposure Analysis:

Based on the chronic dietary exposure analysis as described above and using a cPAD of 0.0006 mg/kg/d for the U.S. population and all population subgroups, chronic dietary exposure to all population subgroups does not exceed the cPAD (<100%; see Table 10). Children 1-6 years have been identified as the most highly exposed population subgroup. The chronic summary table below shows the chronic dietary risks to the U.S. population, infants, and children from exposures to all the supported crops for which endosulfan is registered. A complete listing of the chronic dietary results is in attachment 6.

Table10. Chronic Dietary Risk Estimates with “Weighted” FDA Data

Population	cPAD mg/kg/day	Exposure (mg/kg/day)	% Chronic PAD
U.S. Population	0.0006	0.000046	<1
All Infants (<1 year)	0.0006	0.000060	10
Children 1-6 years	0.0006	0.000115	19
Children 7-12 years	0.0006	0.000071	12
Females 13-50 years	0.0006	0.000033	6
Males 13-19 years	0.0006	0.000048	8
Males 20+ years	0.0006	0.000034	6
Seniors 55+ years	0.0006	0.000033	6

ATTACHMENTS

Attachment 1: Data Used in Revised Probabilistic Dietary Assessment Table
Attachment 2: Anticipated Residues and Residue Data Files for Revised Probabilistic Dietary Assessment
Attachment 3: Revised Acute Residue Information (AC1 file)
Attachment 4: Results of Revised Acute Dietary Exposure Analysis
Attachment 5: Critical Exposure Contribution for Revised Probabilistic Dietary Assessment
Attachment 6: Revised Chronic Residue Information (CH1 file)
Attachment 7: Results of Revised Chronic Dietary Exposure Analysis
Attachment 8: Revised Use Closure Memorandum from SRRD
Attachment 9: Revised Qualitative Usage Analysis (QUA) Report from BEAD

cc: Sherrie L. Kinard (RRB2), Endosulfan Reg. Std. File, Endosulfan Subject File, RF, LAN. RD/I: ChemSAC (10/20/1999); Dietary Exposure SAC (12/7/2000).

7509C: RRB2: S. Kinard: CM#2:Rm 722B: 703-305-0563:2/28/2002.